

MARKED-UP COPY OF AMENDMENT AND RESPONSE TO RESTRICTION
REQUIREMENT

IN THE CLAIMS

Cancel Claims 12-22.

Please amend the claims as follows:

--1. (Amended) A method for determining a nucleotide sequence of a nucleic acid by single dye molecule detection, which comprises [the steps of]:

- (a) immobilizing a nucleic acid molecule, or a primer which has a sequence complementary to a part of the sequence of the nucleic acid molecule, onto the surface of a solid;
- (b) annealing a primer, which has a sequence complementary to a part of the sequence of the nucleic acid molecule, or a nucleic acid molecule to the nucleic acid molecule or the primer, respectively;
- (c) providing a solution which contains DNA polymerase and one type of dye-labeled dNTP [(], where N is A, T or U, G or C)], or RNA polymerase and one type of dye-labeled NTP [(], where N is A, U, G or C)], to said immobilized nucleic acid molecule, and allowing the nucleotide to react with the 3' end of said primer, whereby a nucleotide, which forms a base-pair with a base opposed to the reaction site, is bound to the primer by action of the polymerase;
- (d) detecting a bound, dye-labeled dNTP or NTP;
- (e) disrupting the dye molecule of the bound, dye-labeled dNTP or NTP;

- (f) repeating [said steps (3) to (5)] (c) to (e) while changing the type of dye-labeled dNTP or NTP in turn, to sequentially bind dNTPs or NTPs which forms a base-pair with the nucleotides of the nucleic acid molecule; and
- (g) determining a nucleotide sequence of the nucleic acid molecule based on the types of the sequentially bound dNTPs or NTPs.

3. (Amended) The method of Claim 1, wherein [said step (4)] (d) comprises optically detecting the dye molecule of said dye-labeled dNTP or NTP.

4. (Amended) The method of Claim 1, wherein [said step (4)] (d) comprises exciting dye molecules by irradiation of a laser beam and detecting the thus released fluorescent signal.

6. (Amended) The method of Claim 1, wherein said disruption of dye molecules in [said step (5)] (e) is performed by irradiation of a laser beam stronger than that in [the step (4)] (d). --

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Docket No. 216583US0X CONT
IN RE APPLICATION OF: Tamotsu KONDOW, et al
SERIAL NO: 09/996,591
FILED: November 30, 2001
FOR: METHODS FOR DETERMINING NUCLEOTIDE SEQUENCES OF SINGLE NUCLEIC ACID MOLECULES

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Transmitted herewith is an Preliminary Amendment and Response to Restriction Requirement w/attached marked-up copy in the above-identified application.

- ☒ No additional fee is required
- ☐ Small entity status of this application under 37 C.F.R. §1.9 and §1.27 is claimed.
- ☐ Additional documents filed herewith:

The Fee has been calculated as shown below:

CLAIMS	CLAIMS REMAINING		HIGHEST NUMBER PREVIOUSLY PAID	NO. EXTRA CLAIMS	RATE	CALCULATIONS
TOTAL	14	MINUS	25	0	x \$18 =	\$0.00
INDEPENDENT	2	MINUS	3	0	x \$84 =	\$0.00
		<input type="checkbox"/> MULTIPLE DEPENDENT CLAIMS			+ \$280 =	\$0.00
		TOTAL OF ABOVE CALCULATIONS				\$0.00
		<input type="checkbox"/> Reduction by 50% for filing by Small Entity				\$0.00
		<input type="checkbox"/> Recordation of Assignment			+ \$40 =	\$0.00
		TOTAL				\$0.00

- ☐ A check in the amount of **\$0.00** is attached.
- ☒ Please charge any additional Fees for the papers being filed herewith and for which no check is enclosed herewith, or credit any overpayment to deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.
- ☒ If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. §1.136, and any additional fees required under 37 C.F.R. §1.136 for any necessary extension of time may be charged to Deposit Account No. 15-0030. A duplicate copy of this sheet is enclosed.

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